REMARKS

Claims 51-53 and 70-77 are pending in the application. Claims 1-3, 34-50, 54-69 and 78 have been cancelled. Support for the amendments to claims 51 and 70-77 can be found, *inter alia*, in cancelled claim 49, and in the cancelled claims from which each of claims 51 and 70-77 previously depended. Hence, the amendments to the claims do not constitute new matter, and entry is respectfully requested.

I. Rejection under 35 U.S.C. § 112

Claim 72 has been rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner notes that claim 72 depends from claim 35. The Examiner states that the term "zwitterionic group" in claim 35 is used by the claim to mean "ammonium" or "phosphonium", while the accepted meaning is "a group bearing both a positive and a negative charge." The Examiner thus takes the position that ammonium and phosphonium each bear one negative and no positive charge; hence, the term is indefinite because the specification allegedly does not clearly redefine the term.

The subject matter of claim 35 has been incorporated into claim 72.

Claim 72 has been amended to recite "in which the zwitterionic group comprises ammonium, phosphonium, or sulphonium and phosphate or phosphonate ester…". (See, for example, page 5, starting at line 8.)

Reconsideration and withdrawal of the rejection are earnestly solicited.

II. Rejections under 35 U.S.C. § 102

Claim 51 is rejected under 35 U.S.C. §102(a) and §102(e) as being anticipated by U.S. Patent 6,416,740 to Unger (hereinafter "Unger"). The Office Action asserts that Unger discloses the administration of a composition to an animal, wherein the composition comprises particles of a polymer matrix into which is absorbed aqueous liquid, the particles having diameters in the range of 100 microns to 1 mm (1000 microns), wherein the surface of the particles express zwitterionic lipids. In support of these assertions, the Office Action cites the Abstract; column 4, lines 22-31; column 6, lines 5-8; column 20, line 46; Figures 1-3; and claim 1.

Applicants respectfully traverse the rejection.

Claim 51 incorporates the subject matter of claim 1, and thus recites "comprising particles of a polymer matrix into which is absorbed aqueous liquid." Such a polymer matrix extends throughout the particle, can be porous or non-porous (see page 15, lines 5-15); may be irregular in shape (page 16, lines 7-14); and may be formed by bulk solid or gel (see *id.*).

In contrast, Unger is directed toward therapeutic delivery systems that comprise gaseous precursor filled *vesicles*, e.g., microspheres. A detailed description of Unger's "vesicles" can be found, for example, at column 5, line 33-column 6, line 4. Unger's vesicles are characterized by walls or membranes which form one or more internal voids, and preferably comprise walls formulated from lipids (see *id.*). Moreover, each of Unger's examples refer to lipospheres (see examples and Figures 1-3). Thus, Unger's vesicles only *encapsulate* gas or gaseous precursors, whereas the instantly claimed polymer matrix extends throughout the particle, and is thus is not limited to such a configuration (rather, aqueous liquid is absorbed into a polymer matrix). Accordingly, Unger does not disclose a method of treating an animal in which a composition

having a *polymer matrix* into which aqueous liquid is *absorbed* as being administered to an animal for therapeutic diagnosis.

Unger thus does not anticipate claim 51. Withdrawal of the rejection and allowance of all pending claims are earnestly solicited.

III. Rejections under 35 U.S.C. § 103

A. Claims 51 and 70-78 are rejected under 35 U.S.C. § 103(a) as being unpatentable over JP 11-322948 (hereinafter "JP '948"). The Office Action asserts that JP '948 discloses a therapeutic composition comprising particles of a polymer matrix into which is adsorbed aqueous liquid, the particles having diameters in the range of 1 nm to 100,000 nm (100 microns). To support these assertions, the Office Action cites the Abstract; paragraphs 4-17 and 27-29; and claims 1-3. The Office Action further takes the position that the spherical particles comprise a copolymer of 2-(methacryloyloxy) ethyl 2-(trimethylammonio) ethyl phosphate and n-butyl methacrylate, wherein the zwitterionic 2-(trimethylammonio) ethyl phosphate is expressed on the surface, as is allegedly disclosed cited in paragraphs 27-29. Further, the Office Action states that JP '948 teaches the utility of the composition as a drug delivery system for therapeutic treatment. The Office Action concedes that JP '948 fails to disclose the diameter range 40 to 4000 microns, and fails to disclose administration of the composition to an animal for therapy or diagnosis.

Nonetheless, it would allegedly have been obvious to administer the composition disclosed by JP '948 to an animal for therapeutic treatment, with a reasonable expectation of success, as JP '948 teaches the utility of the composition as a drug delivery system for therapeutic treatment. It would also allegedly have been obvious to find the instantly disclosed diameter range of 40 to 4000 microns through routine experimentation, as the diameter range

disclosed by JP '948 of 1 nm to 100 microns overlaps with this range, in order to produce more effective drug delivery systems.

With specific reference to instant claim 76, the Office Action states that claim 76 depends from instant claim 47, which is directed to the properties of the composition when imbibed with physiological saline at room temperature. Likewise, instant claim 78 depends from instant claim 49, which is directed to the properties of the composition when imbibed with water. Thus, although JP '948 does not expressly disclose all the characteristics and properties of the composition claimed, based on the substantially identical process using identical components, the Office Action states that there is a reasonable basis to believe that the properties claimed in the present invention are inherent in the composition disclosed by JP '948.

Applicants respectfully traverse the rejection.

As amended, instant claim 51 incorporates the subject matter of claim 1, and is also amended to include the features of claim 49 to further recite that the diameters of the particles, when fully imbibed with water, are in the range 150 μm to 3000 μm. Claims 70-77 are amended to depend from claim 51, and thus also incorporate these features. Claim 78 is cancelled.

In contrast, the particles disclosed in JP '948 have a maximum diameter of 100 microns. Accordingly, the Examples in JP '948 disclose a range of particle diameters of 100-170 nm (see paragraphs [0030]-[0032]), each of which are below the claimed range by several orders of magnitude. Hence, the claimed particles have a minimum diameter that is above the maximum diameter disclosed in JP '948.

In view of the foregoing, although the Office Action has suggested that it would have been obvious to select an appropriate particle size for therapeutic treatment, JP '948 clearly discloses a maximum particle size of 100 μm. Applicants thus respectfully submit that it would

not have been obvious to select a particle size that is more than 50% larger than the maximum disclosed in JP '948.

Withdrawal of the rejection and allowance of all pending claims are earnestly solicited.

B. Claims 52-53 are rejected under 35 U.S.C. §103(a) as being unpatentable over JP 11-322948 (hereinafter JP '948) in view of WO 0103666 (hereinafter WO '666) in further view of Ishihara et al (*Polymer Preprints*, 42(2):117-118 (2001)). The Office Action states that the relevant portions of JP '948 are provided above in the rejection of claims 51 and 70-78 under 35 U.S.C. §103(a). The Office Action takes the position that JP '948 fails to teach administering the composition to an animal to form an embolus; however, WO '666 teaches that polymeric materials comprising phosphoryl choline (2-(trimethylammonio) ethyl phosphate) serve as effective embolization materials. To support these assertions, the Office Action cites the Abstract; page 1, lines 6-14; page 6, lines 1-17; and Claim 17. The Office Action further asserts that Ishihara et al teaches the excellent biocompatible and antithrombogenic properties of acrylate copolymers of 2-methacryloyloxyethyl phosphorylcholine (2-(methacryloyloxy) ethyl 2-(trimethylammonio) ethyl phosphate) and their administration to the arteries of a patient. In support of this assertion, the Office Action cites the Experimental Section and Conclusion.

Applicants respectfully traverse the rejection.

The amendments and arguments submitted with respect to claim 51 above, also apply to dependent claim 52 and 53. This rejection is thus overcome for at least the same reasons that are discussed above with respect to particle size.

Applicants agree that JP '948 fails to disclose administering the composition to an animal to form an embolus. However, the compositions described in WO '066 are not in the form of the particulate compositions required by instant claim 51. Rather, the compositions in WO '066 are

administered as liquid precursors which precipitate after administration to form occlusive aggregates of polymer to form a mass. In this regard, the polymeric composition in JP '948 and WO '066 are substantially different because, although JP '948 describes particulate compositions, JP '948 does not describe the formation of agglomerates *in situ* after administration. There would thus have been no reason to have adapted the particulate polymers of JP '948 in the embolization process of WO '066. Moreover, even if an artisan were motivated to make such an adaptation, he would not have used a particulate material to form an embolus, since emboli are made in WO '666 by *in situ* precipitation of liquid compositions administered to a subject.

Ishihara is cited by the Examiner as a disclosing the well-accepted biocompatible and antithrombogenic properties of MPC polymers. However, Ishihara relates to compositions used to coat, for example, vascular prosthesis; hollow fiber membranes for artificial kidney haemodialysis; glucose sensors sensors in microcapilliary chips used in blood analysis; and biodegradable nanoparticles having a diameter around 200 nm. Ishihara nowhere discloses embolic compositions, nor particles having the dimensions recited in instant claim 51.

Applicant submit that, even if the MPC monomers were to be used for the applications described in WO '666, there was no teaching or suggestion to use a particle composition having a particle size within the range recited in instant claim 51. In fact, Ishihara's disclosure is merely cumulative to that of JP '948. MPC polymers are well known to be biocompatible. What was not known at the time of the invention was that particles containing MPC polymers having the sizes defined in claim 51 would have useful properties, e.g., in embolic compositions. This advantage is also non-obvious from the disclosure of WO '866, since WO '066 does not disclose particles of the correct size, nor compositions which are administered with particulate components.

For at least the foregoing reasons, none of claim 51-53 and 70-77 would have been obvious over any combination of JP '948, WO '666, and Ishihara et al.

Withdrawal of the rejections and allowance of all pending claims are earnestly solicited.

III. Conclusion

Withdrawal of the rejection and allowance of all pending claims are earnestly solicited. In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The U.S. Patent and Trademark Office is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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